AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claim 1 (now amended): A pharmaceutical composition effective for the treatment of a *Flaviviridae* infection in a host, comprising an effective amount of a 2'-branched nucleoside, or pharmaceutically acceptable prodrug and/or salt thereof, optionally in a pharmaceutically acceptable carrier or diluent, in combination with one or more drugs that directly or indirectly induce a mutation in a *Flaviviridae* at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region, and/or one or more drugs that are associated with such a mutation.

Claim 2 (previously presented): The pharmaceutical composition of claim 1 wherein the drug is drug that directly or indirectly induces or is associated with a mutation in a *Flaviviridae* at a location other than nucleotide 1214 (G to C) or 405 Ser to Thr of the RNA polymerase region of BVDV or nucleotide 8443 (G to C) of the HCV genome or 282 Ser to Thr of the RNA polymerase region of HCV.

Claim 3 (previously presented): A pharmaceutical composition effective for the treatment of a *Flaviviridae* infection in a host, comprising an effective amount of a 2'-branched nucleoside, or pharmaceutically acceptable prodrug and/or salt thereof, optionally in a pharmaceutically acceptable carrier or diluent, in combination with interferon.

Claim 4 (previously presented): The pharmaceutical composition of claim 3, wherein the interferon is selected from the group consisting of Intron-A (interferon alpha-2b), PEG-INTRON (pegylated interferon alpha-2b), Roferon-A (interferon alfa–2a), PEGASYS (pegylated interferon alfa–2a), INFERGEN (interferon alfacon-1),

OMNIFERON (natural interferon), ALBUFERON, REBIF (interferon beta-1a), Omega Interferon, Oral Interferon Alpha, and Interferon gamma-1b.

Claim 5 (previously presented): The pharmaceutical composition of any one of claims 1-4, wherein the 2'-branched nucleoside is a 2'-branched pyrimidine nucleoside.

Claim 6 (previously presented): The pharmaceutical composition of claim 5, wherein the 2'-branched nucleoside is β-D-2'-CH_3-riboC.

Claim 7 (previously presented): The pharmaceutical composition of claim 5, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β-D-2'-CH_3-riboC.

Claim 8 (previously presented): The pharmaceutical composition of claim 7, wherein the 2'-branched nucleoside is 3'-L-valinyl prodrug of β-D-2'-CH_3-riboC.

Claim 9 (previously presented): The pharmaceutical composition of any one of claims 1-4, wherein the 2'-branched nucleoside is a 2'-branched purine nucleoside.

Claim 10 (previously presented): The pharmaceutical composition of claim 9, wherein the 2'-branched nucleoside is β-D-2'-CH_3-riboA.

Claim 11 (previously presented): The pharmaceutical composition of claim 9, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β-D-2'-CH_3-riboA.

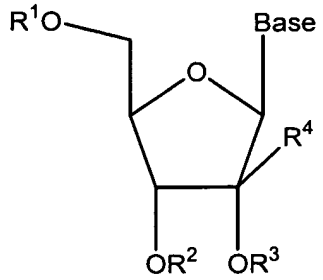
Claim 12 (previously presented): The pharmaceutical composition of claim 11, wherein the 2'-branched nucleoside is a 3'-L-valinyl prodrug of β-D-2'-CH_3-riboA.

Claim 13 (previously presented): The pharmaceutical composition of claim 9, wherein the 2'-branched nucleoside is β-D-2'-CH_3-ribo-6-N-methylaminopurine.

Claim 14 (previously presented): The pharmaceutical composition of claim 9, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β-D-2'-CH_3-ribo-6-N-methylaminopurine.

Claim 15 (previously presented): The pharmaceutical composition of claim 14, wherein the 2'-branched nucleoside is a 3'-L-valinyl prodrug of β-D-2'-CH_3-ribo-6-N-methylaminopurine.

Claim 16 (previously presented): The pharmaceutical compositions of any one of claims 1-4, wherein the 2'-branched nucleoside is of the formula:



or its pharmaceutically acceptable prodrug and/or salt, wherein

R^1, R^2, and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester (including alkyl or arylalkyl sulfonyl including methanesulfonyl); benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; lipid (including a phospholipid); amino acid; carbohydrate; peptide; cholesterol; or a pharmaceutically acceptable leaving group that provides a compound wherein R^1, R^2 or R^3 is independently H or phosphate when administered *in vivo*; and

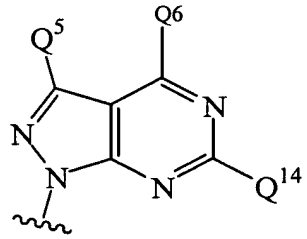
R^4 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, or -N(acyl)$_2$;

and Base is a purine or pyrimidine.

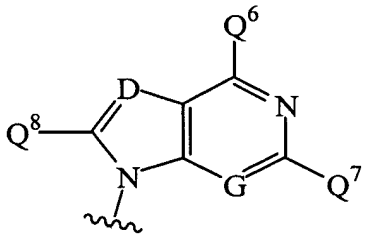
Claim 17 (previously presented): The pharmaceutical composition of claim 16, wherein base is selected from the group consisting of adenine, N^6-alkylpurines, N^6-acylpurines (wherein acyl is C(O)(alkyl, aryl, alkylaryl, or arylalkyl), N^6-benzylpurine, N^6-halopurine, N^6-vinylpurine, N^6-acetylenic purine, N^6-acyl purine, N^6-hydroxyalkyl purine, N^6-thioalkyl purine, N^2-alkylpurines, N^2-alkyl-6-thiopurines, thymine, cytosine, 5-fluorocytosine, 5-methylcytosine, 6-azapyrimidine, including 6-azacytosine, 2- and/or 4-mercaptopyrmidine, uracil, 5-halouracil, including 5-fluorouracil, C^5-alkylpyrimidines, C^5-benzylpyrimidines, C^5-halopyrimidines, C^5-vinyl-pyrimidine, C^5-acetylenic pyrimidine, C^5-acyl pyrimidine, C^5-hydroxyalkyl purine, C^5-amidopyrimidine, C^5-cyanopyrimidine, C^5-nitropyrimidine, C^5-amino-

pyrimidine, N^2-alkylpurines, N^2-alkyl-6-thiopurines, 5-azacytidinyl, 5-aza-uracilyl, triazolopyridinyl, imidazolopyridinyl, pyrrolopyrimidinyl, and pyrazolopyrimidinyl.

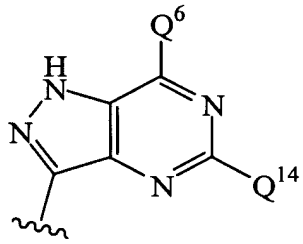
Claim 18 (previously presented): The pharmaceutical composition of claim 16, wherein base is of the formula:



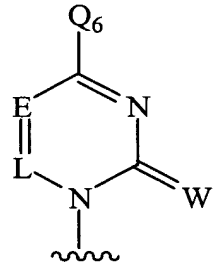
(i)



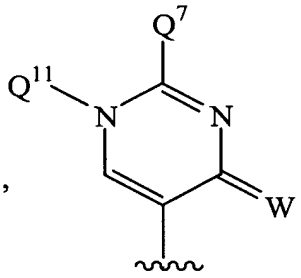
(ii)



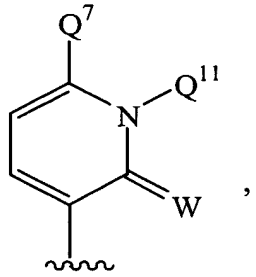
(iii)



(iv)



(v)



(vi)

wherein:

G and L are each independently CH or N;

D is N, CH, C-CN, C-NO_2, C-C_{1-3} alkyl, C-$NHCONH_2$, C-$CONQ^{11}Q^{11}$, C-$CSNQ^{II}Q^{II}$, $CCOOQ^{11}$, C-$C(=NH)NH_2$, C-hydroxy, C-C_{1-3}alkoxy,C-amino, C-C_{1-4}alkyl-amino, C-di(C_{1-4} alkyl)amino, C-halogen, C-(1,3-oxazol-2-yl), C-(1,3-thiazol-2-yl), or C-(imidazol-2-yl); wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, amino, hydroxy, carboxy, and C_{1-3} alkoxy;

E is N or CQ^5;

W is O, S, or NR;

R is H, OH, alkyl;

Q^6 is H, OH, SH, NH_2, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{3-6} cycloalkylamino, halogen,

C_{1-4} alkyl, C_{1-4} alkoxy, or CF_3;

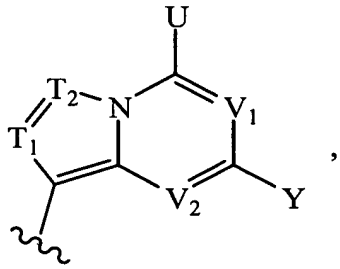
Q^5 is H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} alkylamino, CF_3, halogen, N, CN, NO_2, $NHCONH_2$, $CONQ^{11}Q^{11}$, $CSNQ^{II}Q^{II}$, $COOQ^{11}$, $C(=NH)NH_2$, hydroxy, C_{1-3}alkoxy,amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, halogen, 1,3-oxazol-2-yl, 1,3-thiazol-2-yl, or imidazol-2-yl; wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, amino, hydroxy, carboxy, and C_{1-3} alkoxy;

Q^7 and Q^{14} are each independently selected from the group consisting of H, CF_3, OH, SH, OR, SR C_{1-4} alkyl, amino, C_{1-4} alkylamino, C_{3-6} cycloalkylamino, and di(C_{1-4} alkyl)amino;

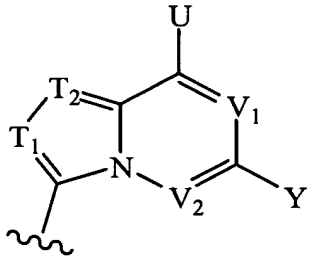
Q^{11} is independently H or C_{1-6} alkyl; and

Q^8 is H, halogen, CN, carboxy, C_{1-4} alkyloxycarbonyl, N_3, amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, hydroxy, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, (C_{1-4} alkyl)$_{0-2}$aminomethyl, NH_2, CN, NO_2, C_{1-3} alkyl, $NHCONH_2$, $CONQ^{11}Q^{11}$, $CSNQ^{II}Q^{II}$, $COOQ^{11}$, $C(=NH)NH_2$, 1,3-oxazol-2-yl, 1,3-thiazol-2-yl, or imidazol-2-yl, wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, amino, hydroxy, carboxy, and C_{1-3} alkoxy.

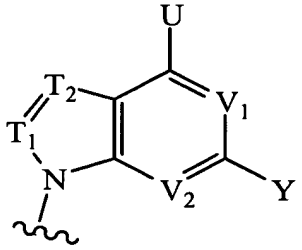
Claim 19 (previously presented): The pharmaceutical composition of claim 16, wherein base is of the formula:



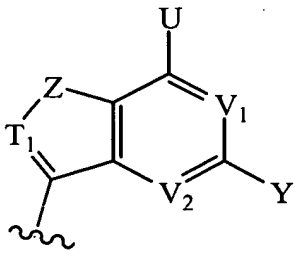
(A)



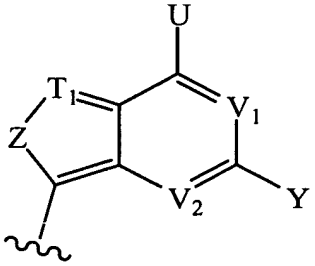
(B)



(C)



(D)



(E)

wherein:

T_1 and T_2 are independently selected from N, CH, or C-Q^{16};

Q^{16}, U, and Y are independently selected from is H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, cycloalkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4R^5 or SR^5, Br-vinyl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-aryl, -O-aralkyl, -O-acyl, -O-cycloalkyl, NH_2, NH-alkyl, N-dialkyl, NH-acyl, N-aryl, N-aralkyl, NH-cycloalkyl, SH, S-alkyl, S-acyl, S-aryl, S-cycloalkyl, S-aralkyl, CN, N_3, COOH, $CONH_2$, CO_2-alkyl, CONH-alkyl, CON-dialkyl, OH, CF_3, CH_2OH, $(CH_2)_mOH$, $(CH_2)_mNH_2$, $(CH_2)_mCOOH$, $(CH_2)_mCN$, $(CH_2)_mNO_2$, $(CH_2)_mCONH_2$, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{3-6} cycloalkylamino, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, (C_{1-4} alkyl)$_{0-2}$aminomethyl, or -NHC(=NH)NH_2;

R^4 and R^5 are independently selected from hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl);

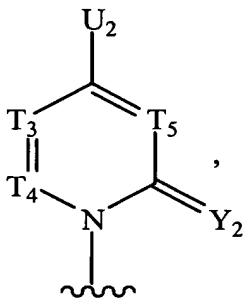
m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

Z is S, SO, SO_2, C=O, or NQ^{20};

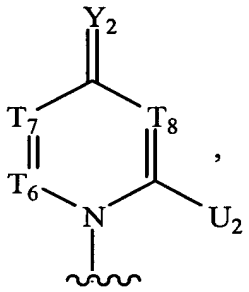
Q^{20} is H or alkyl; and

V_1 and V_2 are independently selected from CH or N.

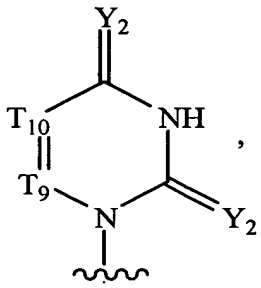
Claim 20 (previously presented): The pharmaceutical composition of claim 16, wherein base is of the formula:



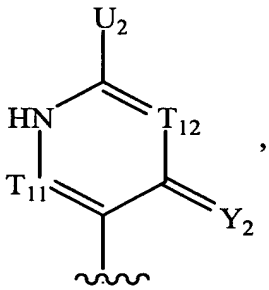
(F)



(G)



(H)



(I)

wherein:

T_3 and T_4 are independently selected from N or CQ^{22};

Q^{22} is independently selected from H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl,

cycloalkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4R^5 or SR^5, Br-vinyl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-aryl, -O-aralkyl, -O-acyl, -O-cycloalkyl, NH_2, NH-alkyl, N-dialkyl, NH-acyl, N-aryl, N-aralkyl, NH-cycloalkyl, SH, S-alkyl, S-acyl, S-aryl, S-cycloalkyl, S-aralkyl, CN, N_3, COOH, $CONH_2$, CO_2-alkyl, CONH-alkyl, CON-dialkyl, OH, CF_3, CH_2OH, $(CH_2)_mOH$, $(CH_2)_mNH_2$, $(CH_2)_mCOOH$, $(CH_2)_mCN$, $(CH_2)_mNO_2$, $(CH_2)_mCONH_2$, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{3-6} cycloalkylamino, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, (C_{1-4} alkyl)$_{0-2}$aminomethyl, or -NHC(=NH)NH_2;

T_5 is NH;

R^4 and R^5 are independently selected from hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl);

m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

T_6, T_7, T_8, T_9, T_{10}, T_{11}, and T_{12} are independently selected from N or CH;

U_2 is H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4R^5 or SR^5;

Y_2 is O, S, NH, NR or $CQ^{24}Q^{26}$ where R is H, OH, or alkyl; and

Q^{24} and Q^{26} are independently selected from H, alkyl, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4R^5 or SR^5.

Claim 21 (now amended): A pharmaceutical composition effective for the treatment of a *Flaviviridae* infection in a host, comprising:

an effective amount of a 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside, or pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier or diluent;

in combination with one or more drugs that directly or indirectly induce a mutation in a *Flaviviridae* at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region, and/or one or more drugs that are associated with such a mutation.

Claim 22 (previously presented): The pharmaceutical composition of claim 21 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is a 2', 3' and/or 5'-prodrug of a 2'-branched pyrimidine nucleoside.

Claim 23 (previously presented): The pharmaceutical composition of claim 22 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 2', 3' and/or 5'-prodrug of β-D-2'-CH_3-riboC.

Claim 24 (previously presented): The pharmaceutical composition of claim 23 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-amino acid prodrug of β-D-2'-CH_3-riboC.

Claim 25 (previously presented): The pharmaceutical composition of claim 24 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-L-valinyl prodrug of β-D-2'-CH_3-riboC.

Claim 26 (previously presented): The pharmaceutical composition of claim 21 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is a 2', 3' and/or 5'-prodrug of a 2'-branched purine nucleoside.

Claim 27 (previously presented): The pharmaceutical composition of claim 26 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 2', 3' and/or 5'-prodrug of β-D-2'-CH_3-riboA.

Claim 28 (previously presented): The pharmaceutical composition of claim 27 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-amino acid prodrug of β-D-2'-CH_3-riboA.

Claim 29 (previously presented): The pharmaceutical composition of claim 28 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-L-valinyl prodrug of β-D-2'-CH_3-riboA.

Claim 30 (previously presented): The pharmaceutical composition of claim 26 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 2', 3' and/or 5'-prodrug of β-D-2'-CH_3-ribo-6-N-methylamino-purine.

Claim 31 (previously presented): The pharmaceutical composition of claim 30 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-amino acid prodrug of β-D-2'-CH_3-ribo-6-N-methylamino-purine.

Claim 32 (previously presented): The pharmaceutical composition of claim 31 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-L-valinyl prodrug of β-D-2'-CH_3-ribo-6-N-methylamino-purine.

Claim 33 (now amended): A method for treating a *Flaviviridae* infection in a host, comprising administering an effective amount of a 2'-branched nucleoside, or its pharmaceutically acceptable prodrug or salt to the host, optionally in a pharmaceutically acceptable carrier or diluent, in combination and/or alternation with one or more drugs that directly or indirectly induce a mutation in a *Flaviviridae* at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region, and/or one or more drugs that are associated with such a mutation.

Claim 34 (previously presented): The method of claim 33 wherein the drug is drug that directly or indirectly induces or is associated with a mutation in a *Flaviviridae* at a location other than nucleotide 1214 (G to C) or 405 Ser to Thr of the RNA polymerase region of BVDV or nucleotide 8443 (G to C) of the HCV genome or 282 Ser to Thr of the RNA polymerase region of HCV.

Claim 35 (previously presented): A method for treating a *Flaviviridae* infection in a host comprising administering an effective amount of a 2'-branched nucleoside, or pharmaceutically acceptable prodrug and/or salt thereof to the host, optionally in a pharmaceutically acceptable carrier or diluent, in combination and/or alternation with interferon.

Claim 36 (previously presented): The method of claim 35, wherein the interferon is selected from the group consisting of Intron-A (interferon alpha-2b), PEG-INTRON (pegylated interferon alpha-2b), Roferon-A (interferon alfa–2a), PEGASYS (pegylated interferon alfa–2a), INFERGEN (interferon alfacon-1), OMNIFERON (natural interferon), ALBUFERON, REBIF (interferon beta-1a), Omega Interferon, Oral Interferon Alpha, and Interferon gamma-1b.

Claim 37 (previously presented): The method of any one of claims 33-36, wherein the 2'-branched nucleoside is a 2'-branched pyrimidine nucleoside.

Claim 38 (previously presented): The method of claim 37, wherein the 2'-branched nucleoside is β-D-2'-CH_3-riboC.

Claim 39 (previously presented): The method of claim 37, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β-D-2'-CH_3-riboC.

Claim 40 (previously presented): The method of claim 39, wherein the 2'-branched nucleoside is 3'-L-valinyl prodrug of β-D-2'-CH_3-riboC.

Claim 41 (previously presented): The method of any one of claims 33-36, wherein the 2'-branched nucleoside is a 2'-branched purine nucleoside.

Claim 42 (previously presented): The method of claim 41, wherein the 2'-branched nucleoside is β-D-2'-CH_3-riboA.

Claim 43 (previously presented): The method of claim 41, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β-D-2'-CH_3-riboA.

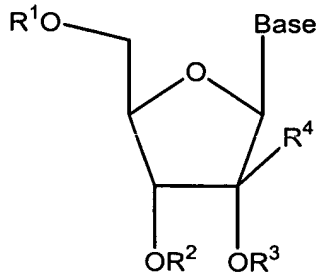
Claim 44 (previously presented): The method of claim 43, wherein the 2'-branched nucleoside is a 3'-L-valinyl prodrug of β-D-2'-CH_3-riboA.

Claim 45 (previously presented): The method of claim 41, wherein the 2'-branched nucleoside is β-D-2'-CH_3-ribo-6-N-methylaminopurine.

Claim 46 (previously presented): The method of claim 41, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β-D-2'-CH_3-ribo-6-N-methylaminopurine.

Claim 47 (previously presented): The method of claim 46, wherein the 2'-branched nucleoside is a 3'-L-valinyl prodrug of β-D-2'-CH_3-ribo-6-N-methylaminopurine.

Claim 48 (previously presented): The method of any one of claims 33-36, wherein the 2'-branched nucleoside is of the formula:



or its pharmaceutically acceptable prodrug and/or salt, wherein

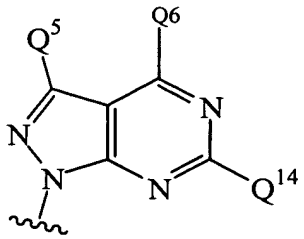
R^1, R^2, and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester (including alkyl or arylalkyl sulfonyl including methanesulfonyl); benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; lipid (including a phospholipid); amino acid; carbohydrate; peptide; cholesterol; or a pharmaceutically acceptable leaving group that provides a compound wherein R^1, R^2 or R^3 is independently H or phosphate when administered *in vivo*; and

R^4 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, or -N(acyl)$_2$;

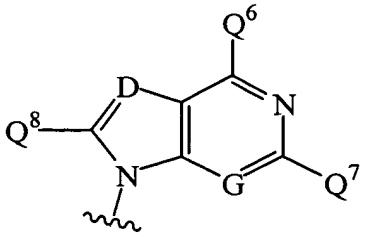
and Base is a purine or pyrimidine.

Claim 49 (previously presented): The method of claim 48, wherein base is selected from the group consisting of adenine, N^6-alkylpurines, N^6-acylpurines (wherein acyl is C(O)(alkyl, aryl, alkylaryl, or arylalkyl), N^6-benzylpurine, N^6-halopurine, N^6-vinylpurine, N^6-acetylenic purine, N^6-acyl purine, N^6-hydroxyalkyl purine, N^6-thioalkyl purine, N^2-alkylpurines, N^2-alkyl-6-thiopurines, thymine, cytosine, 5-fluorocytosine, 5-methylcytosine, 6-azapyrimidine, including 6-azacytosine, 2- and/or 4-mercaptopyrmidine, uracil, 5-halouracil, including 5-fluorouracil, C^5-alkylpyrimidines, C^5-benzylpyrimidines, C^5-halopyrimidines, C^5-vinyl-pyrimidine, C^5-acetylenic pyrimidine, C^5-acyl pyrimidine, C^5-hydroxyalkyl purine, C^5-amidopyrimidine, C^5-cyanopyrimidine, C^5-nitropyrimidine, C^5-amino-pyrimidine, N^2-alkylpurines, N^2-alkyl-6-thiopurines, 5-azacytidinyl, 5-aza-uracilyl, triazolopyridinyl, imidazolopyridinyl, pyrrolopyrimidinyl, and pyrazolopyrimidinyl.

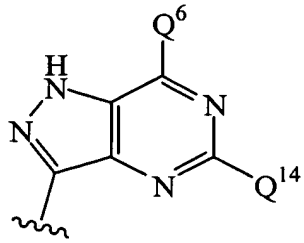
Claim 50 (previously presented): The method of claim 49, wherein base is of the formula:



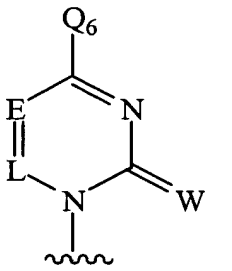
(i)



(ii)



(iii)



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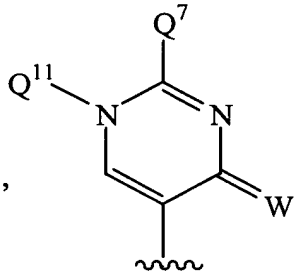

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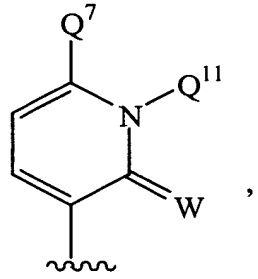


,

(iv) (v) (vi)

wherein:

G and L are each independently CH or N;

D is N, CH, C-CN, C-NO_2, C-C_{1-3} alkyl, C-$NHCONH_2$, C-$CONQ^{11}Q^{11}$, C-$CSNQ^{II}Q^{II}$, $CCOOQ^{11}$, C-$C(=NH)NH_2$, C-hydroxy, C-C_{1-3}alkoxy,C-amino, C-C_{1-4}alkyl-amino, C-di(C_{1-4} alkyl)amino, C-halogen, C-(1,3-oxazol-2-yl), C-(1,3-thiazol-2-yl), or C-(imidazol-2-yl); wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, amino, hydroxy, carboxy, and C_{1-3} alkoxy;

E is N or CQ^5;

W is O, S, or NR;

R is H, OH, alkyl;

Q^6 is H, OH, SH, NH_2, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{3-6} cycloalkylamino, halogen,

C_{1-4} alkyl, C_{1-4} alkoxy, or CF_3;

Q^5 is H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} alkylamino, CF_3, halogen, N, CN, NO_2, $NHCONH_2$, $CONQ^{11}Q^{11}$, $CSNQ^{II}Q^{II}$, $COOQ^{11}$, $C(=NH)NH_2$, hydroxy, C_{1-3}alkoxy,amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, halogen, 1,3-oxazol-2-yl, 1,3-thiazol-2-yl, or imidazol-2-yl; wherein alkyl is unsubstituted or substituted

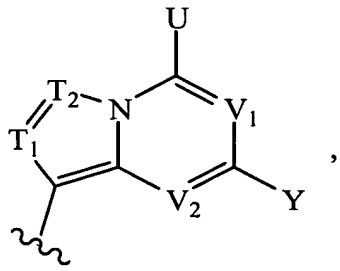
with one to three groups independently selected from halogen, amino, hydroxy, carboxy, and C_{1-3} alkoxy;

Q^7 and Q^{14} are each independently selected from the group consisting of H, CF_3, OH, SH, OR, SR C_{1-4} alkyl, amino, C_{1-4} alkylamino, C_{3-6} cycloalkylamino, and di(C_{1-4} alkyl)amino;

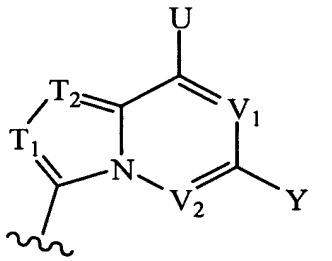
Q^{11} is independently H or C_{1-6} alkyl; and

Q^8 is H, halogen, CN, carboxy, C_{1-4} alkyloxycarbonyl, N_3, amino, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, hydroxy, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, (C_{1-4} alkyl)$_{0-2}$aminomethyl, NH_2, CN, NO_2, C_{1-3} alkyl, $NHCONH_2$, $CONQ^{11}Q^{11}$, $CSNQ^{II}Q^{II}$, $COOQ^{11}$, $C(=NH)NH_2$, 1,3-oxazol-2-yl, 1,3-thiazol-2-yl, or imidazol-2-yl, wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, amino, hydroxy, carboxy, and C_{1-3} alkoxy.

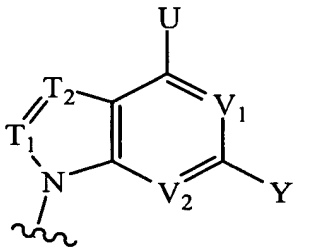
Claim 51 (previously presented): The method of claim 49, wherein base is of the formula:



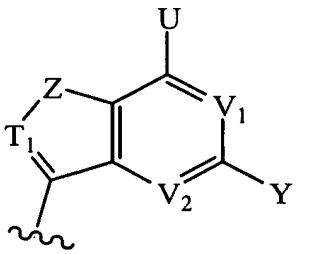
(A)



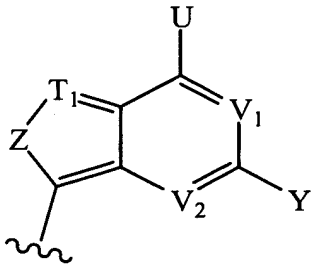
(B)



(C)



(D)



(E)

wherein:

T_1 and T_2 are independently selected from N, CH, or C-Q^{16};

Q^{16}, U, and Y are independently selected from is H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, cycloalkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4R^5 or SR^5, Br-vinyl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-aryl, -O-aralkyl, -O-

acyl, -O-cycloalkyl, NH_2, NH-alkyl, N-dialkyl, NH-acyl, N-aryl, N-aralkyl, NH-cycloalkyl, SH, S-alkyl, S-acyl, S-aryl, S-cycloalkyl, S-aralkyl, CN, N_3, COOH, $CONH_2$, CO_2-alkyl, CONH-alkyl, CON-dialkyl, OH, CF_3, CH_2OH, $(CH_2)_mOH$, $(CH_2)_mNH_2$, $(CH_2)_mCOOH$, $(CH_2)_mCN$, $(CH_2)_mNO_2$, $(CH_2)_mCONH_2$, C_{1-4} alkylamino, di(C_{1-4} alkyl)amino, C_{3-6} cycloalkylamino, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, (C_{1-4} alkyl)$_{0-2}$aminomethyl, or $-NHC(=NH)NH_2$;

R^4 and R^5 are independently selected from hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl);

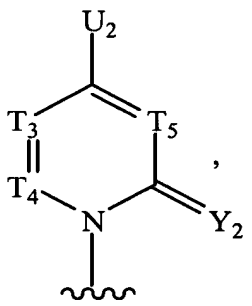
m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

Z is S, SO, SO_2, C=O, or NQ^{20};

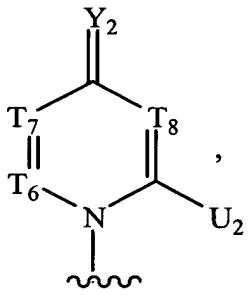
Q^{20} is H or alkyl; and

V_1 and V_2 are independently selected from CH or N.

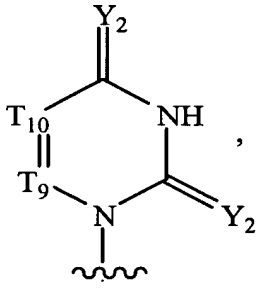
Claim 52 (previously presented): The method of claim 49, wherein base is of the formula:



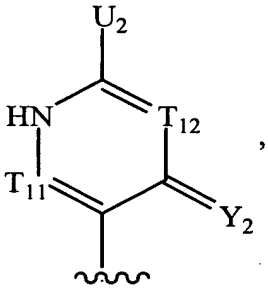
(F)



(G)



(H)



(I)

wherein:

T_3 and T_4 are independently selected from N or CQ^{22};

Q^{22} is independently selected from H, OH, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, cycloalkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4R^5 or SR^5, Br-vinyl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-aryl, -O-aralkyl, -O-acyl, -O-cycloalkyl, NH_2, NH-alkyl, N-dialkyl, NH-acyl, N-aryl, N-aralkyl, NH-cycloalkyl, SH, S-alkyl, S-acyl, S-aryl, S-cycloalkyl, S-aralkyl, CN, N_3, COOH, $CONH_2$, CO_2-alkyl, CONH-alkyl, CON-dialkyl, OH, CF_3, CH_2OH, $(CH_2)_mOH$, $(CH_2)_mNH_2$, $(CH_2)_mCOOH$, $(CH_2)_mCN$, $(CH_2)_mNO_2$, $(CH_2)_mCONH_2$, C_{1-4}

alkylamino, di(C_{1-4} alkyl)amino, C_{3-6} cycloalkylamino, C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, C_{1-6} alkylthio, C_{1-6} alkylsulfonyl, (C_{1-4} alkyl)$_{0-2}$aminomethyl, or -NHC(=NH)NH_2;

T_5 is NH;

R^4 and R^5 are independently selected from hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl);

m is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

T_6, T_7, T_8, T_9, T_{10}, T_{11}, and T_{12} are independently selected from N or CH;

U_2 is H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4R^5 or SR^5;

Y_2 is O, S, NH, NR or $CQ^{24}Q^{26}$ where R is H, OH, or alkyl; and

Q^{24} and Q^{26} are independently selected from H, alkyl, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4R^5 or SR^5.

Claim 53 (previously presented): A method for treating a patient infected with a *Flaviviridae* virus that is resistant to a 2'-branched nucleoside comprising administering an effective amount of interferon, optionally in a pharmaceutically acceptable carrier or diluent, optionally in a manner that substantially eliminates the viral load.

Claim 54 (now amended): A method for treating a patient infected with *Flaviviridae* comprising:

administering an effective amount of a 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside, or pharmaceutically acceptable salt thereof, optionally in a pharmaceutically acceptable carrier or diluent;

in combination and/or alternation with one or more drugs that directly or indirectly induce a mutation in a *Flaviviridae* at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT(Sequence ID No. 63), of domain B of the RNA polymerase region, and/or one or more drugs that are associated with such a mutation.

Claim 55 (previously presented): The method of claim 54, wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is a 2', 3' and/or 5'-prodrug of a 2'-branched pyrimidine nucleoside.

Claim 56 (previously presented): The method of claim 55, wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 2', 3' and/or 5'-prodrug of β-D-2'-CH_3-riboC.

Claim 57 (previously presented): The method of claim 56, wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-amino acid prodrug of β-D-2'-CH_3-riboC.

Claim 58 (previously presented): The method of claim 57, wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-L-valinyl prodrug of β-D-2'-CH_3-riboC.

Claim 59 (previously presented): The method of claim 54 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is a 2', 3' and/or 5'-prodrug of a 2'-branched purine nucleoside.

Claim 60 (previously presented): The method of claim 59 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 2', 3' and/or 5'-prodrug of β-D-2'-CH_3-riboA.

Claim 61 (previously presented): The method of claim 60 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-amino acid prodrug of β-D-2'-CH_3-riboA.

Claim 62 (previously presented): The method of claim 61 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-L-valinyl prodrug of β-D-2'-CH_3-riboA.

Claim 63 (previously presented): The method of claim 59 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 2', 3' and/or 5'-prodrug of β-D-2'-CH_3-ribo-6-N-methylamino-purine.

Claim 64 (previously presented): The method of claim 63 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-amino acid prodrug of β-D-2'-CH_3-ribo-6-N-methylamino-purine.

Claim 65 (previously presented): The method of claim 64 wherein the 2', 3' and/or 5'-prodrug of a 2'-branched nucleoside is 3'-L-valinyl prodrug of β-D-2'-CH_3-ribo-6-N-methylamino-purine.

Claim 66 (previously presented): A method for treating a patient infected with *Flaviviridae* comprising:

(a) administering to the patient an effective amount of a 2'-branched nucleoside, or a pharmaceutically acceptable salt or prodrug thereof; optionally in a pharmaceutically acceptable carrier or diluent;

(b) assaying the blood of the patient to test for seroconversion from wildtype to mutant virus;

(c) administering an effective amount of interferon; optionally in a pharmaceutically acceptable carrier or diluent.

Claim 67 (previously presented): A method for treating a patient infected with *Flaviviridae* comprising:

(a) administering an effective amount of a 2'-branched nucleoside, or pharmaceutically acceptable salt or prodrug thereof; optionally in a pharmaceutically acceptable carrier or diluent;

(b) obtaining a viral sample from the patient;

(c) determining the replication fitness of the virus;

(d) determining whether the replication fitness of the virus in the sample is less than the replication fitness of the wild-type virus, which indicates resistance to β-D-2'-CH_3-riboC;

(e) administering an effective amount of interferon to those patients that are resistant to β-D-2'-CH_3-riboC.

Claim 68 (previously presented): A method for treating a patient infected with *Flaviviridae* comprising:

(a) administering an effective amount of a 2'-branched nucleoside, or pharmaceutically acceptable salt or prodrug thereof; optionally in a pharmaceutically acceptable carrier or diluent;

(b) obtaining a viral culture sample from the patient;

(c) culturing the sample and comparing the plaque growth between the sample and wild type virus;

(d) determining whether the plaque growth of the sample is smaller than the plaque growth of the wildtype, which indicates resistance to β-D-2'-CH_3-riboC;

(e) administering an effective amount of interferon to those patients that are resistant to β-D-2'-CH_3-riboC.

Claim 69 (previously presented): The method of any one of claims 66-68, wherein the 2'-branched nucleoside is a 2'-branched pyrimidine nucleoside.

Claim 70 (previously presented): The method of claim 69, wherein the 2'-branched nucleoside is β-D-2'-CH_3-riboC.

Claim 71 (previously presented): The method of claim 69, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β-D-2'-CH_3-riboC.

Claim 72 (previously presented): The method of claim 71, wherein the 2'-branched nucleoside is 3'-L-valinyl prodrug of β-D-2'-CH_3-riboC.

Claim 73 (previously presented): The method of any one of claims 66-68, wherein the 2'-branched nucleoside is a 2'-branched purine nucleoside.

Claim 74 (previously presented): The method of claim 73, wherein the 2'-branched nucleoside is β-D-2'-CH_3-riboA.

Claim 75 (previously presented): The method of claim 73, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β-D-2'-CH_3-riboA.

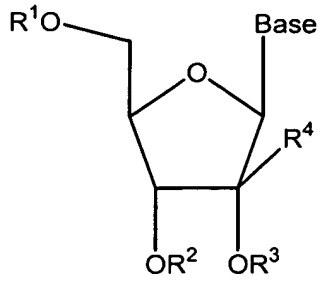
Claim 76 (previously presented): The method of claim 75, wherein the 2'-branched nucleoside is a 3'-L-valinyl prodrug of β-D-2'-CH_3-riboA.

Claim 77 (previously presented): The method of claim 73, wherein the 2'-branched nucleoside is β-D-2'-CH_3-ribo-6-N-methylaminopurine.

Claim 78 (previously presented): The method of claim 73, wherein the 2'-branched nucleoside is a 3'-amino acid prodrug of β-D-2'-CH_3-ribo-6-N-methylaminopurine.

Claim 79 (previously presented): The method of claim 78, wherein the 2'-branched nucleoside is a 3'-L-valinyl prodrug of β-D-2'-CH_3-ribo-6-N-methylaminopurine.

Claim 80 (previously presented): The method of any one of claims 66-68, wherein the 2'-branched nucleoside is of the formula:



or its pharmaceutically acceptable prodrug and/or salt, wherein

R^1, R^2, and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester (including alkyl or arylalkyl sulfonyl including methanesulfonyl); benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; lipid (including a phospholipid); amino acid; carbohydrate; peptide; cholesterol; or a pharmaceutically acceptable leaving group that provides a compound wherein R^1, R^2 or R^3 is independently H or phosphate when administered *in vivo*; and

R^4 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, or -N(acyl)$_2$;

and Base is a purine or pyrimidine.

Claim 81 (now amended): A method for assaying a sample suspected of containing a *Flaviviridae* resistant to a 2'-branched nucleoside comprising:

(a) contacting a sample containing a *Flaviviridae* nucleic acid sequence with a detectable oligonucleotide probe having a sequence complimentary a codon that encodes a serine in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region of *Flaviviridae*;

(b) allowing the probe to hybridize to the sequence;

(c) detecting the hybridization of the probe the sequence.

Claim 82 (previously presented): A method for assaying a sample suspected of containing a *Flaviviridae* resistant to a 2'-branched nucleoside comprising:

(a) contacting a sample containing a *Flaviviridae* nucleic acid sequence with a detectable oligonucleotide probe having a sequence complimentary to the cytidine at nucleotide 1214 of the RNA polymerase region of BVDV or the cytidine at nucleotide 8443 of HCV;

(b) allowing the probe to hybridize to the sequence;

(c) detecting the hybridization of the probe to cytidine at nucleotide 1214 of the RNA polymerase region of BVDV or at nucleotide 8443 of HCV.

Claim 83 (now amended): A kit for assaying a sample suspected of containing a *Flaviviridae* resistant to a 2'-branched nucleoside comprising:

(a) a sample containing a *Flaviviridae* nucleic acid sequence with a detectable oligonucleotide probe having a sequence complimentary a codon that encodes a serine in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region of *Flaviviridae*;

(b) a means for detecting the hybridization of the probe the sequence; and

(c) optionally with instructional material.

Claim 84 (previously presented): A kit for assaying a sample suspected of containing a *Flaviviridae* resistant to a 2'-branched nucleoside comprising:

(a) a sample containing a *Flaviviridae* nucleic acid sequence with a detectable oligonucleotide probe having a sequence complimentary to the cytidine at nucleotide 1214 of the RNA polymerase region of BVDV or the cytidine at nucleotide 8443 of HCV;

(b) a means for detecting the hybridization of the probe to cytidine at nucleotide 1214 of the RNA polymerase region of BVDV or at nucleotide 8443 of HCV; and

(c) optionally with instructional material.

Claim 85 (now amended): A method for diagnosing the presence of *Flaviviridae* resistant to a 2'-branched nucleoside in a patient comprising:

(a) obtaining a sample suspected of containing a Flaviviridae nucleic acid sequence;
(b) contacting the sample with a detectable oligonucleotide probe having a sequence complementary a codon that encodes a serine in the highly conserved consensus sequence, XRXSGXXXT (Sequence ID No. 63), of domain B of the RNA polymerase region of *Flaviviridae*;
(b) allowing the probe to hybridize to the sequence; and
(c) detecting the hybridization of the probe the sequence to determine the presence of a β-D-2'-CH_3-riboC-resistant *Flaviviridae*.

Claim 86 (previously presented): A method for diagnosing the presence of a *Flaviviridae* resistant to a 2'-branched nucleoside in a patient comprising:

(a) obtaining a sample suspected of containing a Flaviviridae nucleic acid sequence;
(b) contacting the sample with a detectable oligonucleotide probe having a sequence complementary to the cytidine at nucleotide 1214 of the RNA polymerase region of BVDV or the cytidine at nucleotide 8443 of HCV;
(b) allowing the probe to hybridize to the sequence; and
(c) detecting the hybridization of the probe to cytidine at nucleotide 1214 of the RNA polymerase region of BVDV or at nucleotide 8443 of HCV to determine the presence of a β-D-2'-CH_3-riboC-resistant *Flaviviridae*.